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EXAMINER	
PORTNER, VIRGINIA ALLEN	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/607,834	VOGEL ET AL.	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-85* is/are pending in the application.

4a) Of the above claim(s) *3,5,10-15 and 26-85* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2,4,6-9,16-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-85 are pending.
Claims 1-2,4,6-9,16-25 are under consideration.
1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Allowable Subject Matter

1. No single claim recites Applicant's originally elected species*:*

Applicant's election with traverse of Group I, in the reply filed on January 10, 2007 is acknowledged, wherein the species elected for examination is

a method of **changing the binding strength** between an adhesion molecule and its binding ligand, classified in class 422, subclass 186: the species combination being:

Increase change in bond stress

Shear force

FimH polypeptide (clams 8-9)

Mannose (free or attached to a particle, monomannose, trimannose or oligomannose)

Mannose attached to bacterial pili While the elected species is encompassed by the genus claims pending, no single claim recites the specific species elected for examination and previously indicated as allowable. The examiner would like to see a claim directed to the elected species that defines over the prior art of record that specifically recited the elected combination of claim limitations. Applicant's elected species directed to a method that results in an increased change in bond stress, through Shear force, the bond being between a FimH polypeptide (claims 18) attached to a bacterial pili carrier particle and Mannose attached to a bacterial pili carrier particle (claim 20), this species defines over the prior art of record.

2. ***Specification Objection Withdrawn:*** The disclosure objected to because it contains an embedded hyperlink and/or other form of browser-executable code, has been obviated by amendment of the Specification to remove the hyperlinks. Additionally the figures have been amended to no longer refer to colored ball and stick residues and these features have been numbered as the figures are published in black and white, therefore the narrative will be clear when published.

3. ***Withdrawn, Claim Objections*** Claim 21 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim, has been obviated in light of Applicant's traversal.

4. ***Withdrawn Claim Rejections - 35 USC § 112,*** Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements in light of the amendment of claim 1.

5. ***Withdrawn Claim Rejections*** Claim 20 is no longer rejected under 35 USC 112, second paragraph for not providing is insufficient antecedent basis for the recited claim limitations in light of the amendment of claim 1 and traversal made of record by Applicant's representative.

Response to Arguments

6. Applicant's arguments filed September 17, 2007 have been fully considered but they are not persuasive.

7. ***Rejections Maintained, Claim Rejections - 35 USC § 102:*** The rejection of claims 1-2,4,6-9,16-17,18, 19-21, 22-25 under 35 U.S.C. 102(b) as being anticipated by Pascual et al (WO97/18790) in light of Spevak et al 1996 incorporated by reference (particle attached carbohydrate) is traversed on the grounds that:

a. Pascual and Spevak do not describe every element of claim 1 as amended; and

b. the cited references do not exactly describe the invention as now claimed.

8. It is the position of the examiner that the claims as amended recite a combination of I-FABSDAM and FAMSDB-L, which are defined in the instant Specification to represent a genus of adhesion molecules and a genus of corresponding ligand/receptor molecules:

"[0110] FABSDAMs useful in the practice of this invention include naturally-occurring and isolated **adhesins, selectins, and integrins, and adhesion molecules including members of the immunoglobulin superfamily** and syndecans that are capable of binding in a force-activated bond stress-dependent manner that are known to the art and that are as yet to be discovered. Adhesins useful in the practice of this invention include FimH polypeptides and the lectin domains of FimH polypeptides. FimH can be from E. coli. A FimH useful in the practice of this invention

has a polypeptide sequence of Genbank Accession Number P08191. FimH polypeptides useful in the practice of this invention include naturally occurring FimH variants and engineered FimH polypeptides containing mutations including mutations affecting the force-activated bond stress-dependent binding properties. Naturally occurring FimH variants include FimHs in E. coli strains f-18 and j-96. Engineered FimH polypeptides include FimH polypeptides having a valine at amino acid position 27, a proline at any of positions 154-156, a leucine at position 32, or an alanine at position 124. FABSDB-Ls useful in the practice of this invention include fructoses, mannoses including monomannose, trimannose, and oligomannose, and all other FABSDB-Ls that bind to FABSDAMs in a force-activated bond stress-dependent manner.

[0111] In the practice of this invention, a FABSDAM or an isolated FABSDAM (I-FABSDAM) and/or a FASBSDB-L can be attached to a particle, including, but not limited to bacterial pili, naturally occurring isolated molecules, synthetic molecules, proteins, polypeptides, organelles, prokaryotic cells to which said FABSDAM is not native, eukaryotic cells to which said I-FABSDAM is not native, viruses, **organisms**, nanoparticles, microbeads, and microparticles or to a **surface selected from the group consisting of cell membranes**, other biological membranes, device surfaces and synthetic substrate surfaces. Both a FABSDAM and a FASBSDB-L can be attached to the same particle or surface. Methods for attaching proteins and ligands to particles and surfaces are known in the art.

Definitions

[0142] As used herein, "force-activated bond stress-dependent adhesion molecule" and "**FABSDAM" refer to molecules that are capable of binding ligands in a force-activated bond stress-dependent manner**. FABSDAMs include, but are not limited to, adhesins, selectins, and integrins. Adhesion molecules include adhesins, selecting, integrins, cadherins, immunoglobulin superfamily cell adhesion molecules, and syndecans (Hauck C. R. (2002) Med Microbiol. Immuno. 191:55-62). FimH proteins are adhesins of bacterial origin. FimH polypeptides include all proteins that are structurally and functionally similar to bacterial derived FimH proteins, including, but not limited to all natural bacterial FimH variants, purified natural FimH proteins, engineered FimH polypeptides, mutated FimH polypeptides, chemically synthesized FimH polypeptides, and truncated but functional portions that are polypeptides of FimH proteins such as the lectin domain. FimH sequences can be found at GenBank Accession Nos. X05672 and AF288194. Methods for purifying FimH are known in the art (see Jones, 1995). As used herein, "isolated force-activated bond stress-dependent binding adhesion molecule" and "I-FABSDAM" refer to FABSDAMs that are not in the same context in which they exist in nature, including their natural in vivo context. All I-FABSDAMs are FABSDAMs. An E. coli that naturally has FimH-j96 protein, a naturally occurring variant of FimH, that has been transformed with an engineered FimH-f18 gene, isolated from a naturally occurring E. coli variant, and expresses FimH-f18, comprises two FABSDAMs but only one I-FABSDAM. Both FimH-j96 protein and FimH-f18 protein are FABSDAMs, but only the engineered and transformed FimH-f18 protein is an I-FABSDAM in this example. Even if the FimH-f18 (FimH-f18 is a natural strain) protein has the same sequence as the naturally occurring variant, because it is not in the in vivo context in which it is found in nature, it is isolated. Adhesins also include extracellular matrix adhesins, for example collagen adhesins of S. aureus which bind to collagen. "

Therefore, in light of Applicant's definitions of the terms recited in the instant claims, Pascual et al still anticipates the instantly claimed invention because Pascual et al disclose molecules that are adhesins (selectins) binding to ligands on the surfaces of cell membranes. Instant claim1 is not limited to a method of evaluating bacterial adhesins bond strength but encompasses eukaryotic adhesins in association with cell membrane associated ligands, the

bonds of which are changed due to shear stress. While Pascual evaluates competitive inhibitors of known adhesion/ligand binding strength under shear forces, these competitive inhibitors meet the definition provided in Applicant's specification which defines the adhesion molecule to be "FABSDAM" refer to **molecules that are capable of binding ligands in a force-activated bond stress-dependent manner**." The method of Pascual et al in light Spevak et al still anticipates the instantly claimed invention as now claimed.

Original prior art rejection: Pascual et al disclose the instantly claimed method, the method comprising the step (see page 12, lines 15-33; page 30, lines 33-36 "an in vitro shear assay system"; "Assessment of the adhesivity of pathogens with target cell receptors under different levels of shear force (see page 31, lines 10-19)" , see page 41 of : **Instant claim 1,22, 25**: Changing a bond stress of an isolated force activated bond stress dependent adhesion molecule (see page 60 line 17 "purified"; page 64, lines 21-22 "purified adhesion of adhesion-positive microbes"; page 16, Table 1, and lines 6-7 "in vitro assays under high shear conditions designed to reflect blood flow"; E-selectin; P-selectin; L-selectin binding to ligands on endothelium or leukocytes, wherein binding increases in the presence of shear force (shear, positive binding) and decreases in the absence of shear forces ("static" and negative binding).

to a force activated bond stress dependent binding ligand; protein-carbohydrate interactions (see page 13, lines 9-10) ; "different glycoconjugates that function as counter-receptors for pathogen adhesion molecules" (page 19, lines 31-32); also see page 32, lines 18-27 "adhesion molecule of a pathogenic organism which interacts with receptor molecules of a cell); "multivalent assemblies displaying carbohydrate ligands (page 59, lines 31-32).

Instant claim 2: wherein the bond stress is shear force (see page 16, Table 1, and lines 6-7 "in vitro assays under high shear conditions designed to reflect blood flow";

Instant claim 4: binding increases in the presence of shear force (shear, positive binding) and decreases in the absence of shear forces ("static" and negative binding). (see page 16, Table).

Instant claim 6: wherein the method results in tightly bound adhesion and ligand binding (See page 17 "shear-dependent attachment and rolling".; "activation dependent adhesion strengthening (slowed rolling), followed by tight adhesion").

Instant claim 7: wherein the adhesion molecule is microbial lectins (see page 17, lines 16-30), or an adhesin, selectin, integrin, immunoglobulin superfamily cell adhesion molecule or microbial lectin

Instant claim 8: wherein the adhesion comprises polypeptide (see claim 30, "the adhesive lectin region on fibriae displayed on microbes selected from the group consisting of Escherichia coli, Neisseria gonorrhoeae, Neisseria meningitides, Salmonella typhi, Salmonella typhimurium, Pseudomonas aeruginosa and Yersinia enterocolitica, page 87 and page 71, Salmonella typhi and typhimurium, fimbrial adhesion binds to mannose, and is therefore a FimH polypeptide. polypeptide). "Lectins frequently appear on the surface of the cell, on specific organelles, such as bacterial fimbriae or are part of the structure of exotoxins elaborated by bacteria."

Instant claim 9: wherein the FimH polypeptide is an E.coli FimH polypeptide (see page 71, E.coli binding to mannose, and therefore is a FimH, E.coli polypeptide). While the reference does not mention the term "FimH", in light of evidence provided by Swiss-Prot accession numbers P08191 and Q9R5Y2 that show both E.coli and Salmonella to express a polypeptide that binds to mannose and is referred to as FimH.

Instant claim 16-17: mannose or oligomannose (see mono or oligosaccharide, both simple or complex (page 11, lines 35-36; and page 71, carbohydrate specificity column "Mannose"). see page 11, lines 35-36 and page 12, lines 1-7 "Lectins bind reversibly and noncovalently with mono or oligosaccharides, both simple and complex" and page 72, lines 16-17).

Instant claim 18: wherein the adhesion molecule is attached to a particle, the particle being a bacterial pili (also known as Fimbrial adhesion, see page 71) being "bead-bound"(see page 41, lines 16-17); see "E.coli coated beads (see page 44, line 40), or "purified glycoproteins" that are incorporated into screening matrices (see page 60, lines 16-22 and page 61) thus producing a synthetic molecule associated with a synthetic substrate surface.

Instant claim 19: wherein the ligand is attached to a particle (see page 59, Example 14 "carbohydrate terminated matrices" in light of Spevak et al, 1996, incorporated by reference) purified ligand coated on the luminal surface of a capillary tube reaction chamber" see page 56, lines 28-31)

Instant claim 20-21: ligand attached to a particle, the particle being a synthetic molecule (in light of teaching by Spevak et al incorporated by reference, particles), or coated on a device surface which is a synthetic substrate surface.

Instant claims 23-25: wherein changing said bond stress comprises applying a bond stress within the claimed ranges of 1-3 dynes/cm^2 (see page 41, line 8).

Pascual et al anticipates the instantly claimed invention directed to a method that increases bond strength by of a bacterial lectin adhesins present in purified fimbria of Salmonella and E.coli that bind to mannose or oligomannose ligands each of which are attached to a particle, in light of Spevak (1996, incorporated into Pascual et al by reference, page 59, lines 29-30) that teach particles for attaching carbohydrate ligands.

1. Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594

2. Inherently the reference anticipates the now claimed invention. Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states AArtisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior arts functioning, does not render the old composition patentably new to the discoverer. The Court further held that Athis same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art.

1. The rejection of claims 1-2,4,6-9,16-17,18, 19-21, 22-25 under 35 U.S.C. 102(e) as being anticipated by Bargatze et al, (US PG Pub. 2004/0247611, effective filing date November 23, 1998) is traversed on the grounds that:

a. Bargatze et al does not describe every element of the claimed invention, specifically the reference "fails to disclose an isolated force activated stress dependent adhesion molecule (I-FABSDAM) or a force activated bond stress dependent binding ligand (FABSDB-L)" and concludes that "the cited reference does not exactly describe the invention as now claimed."

b. Bargatze shows an assay that evaluates the interaction between the pathogen adhesion molecule and its corresponding ligand to identify a pathogen.

2. It is the position of the examiner that the terms (I-FABSDAM) and (FABSDB-L) are terms that are defined in the Specification to represent a genus of molecules with specific functional characteristics; the functional characteristics being adhesion activity and adhesion binding activity, respectively. The instant method requires the (I-FABSDAM) and the (FABSDB-L) to bind to each other and for the bond stress to be changed, the change including increased binding strength under shear flow conditions. One mode of increasing bond stress defined, as defined in the instant Specification, is flow bond stress induced changes.
Prior art rejection: Bargatze et al disclose and claim a method of increasing the bond strength of an adhesion molecule (see page 25, claims 55-56 "soluble pathogen adhesins" introduced to a moving fluid that creates shear flow conditions), wherein the adhesins are contacted with carbohydrate ligands coated on beads (see page 25, claims 65-66 "carbohydrate"), the method comprising the step of :

binding the adhesion with the ligand :

"(55. A method for identifying pathogen-ligand adhesive interactions under shear flow conditions, wherein the ligand is immobilized on a substrate.

56. The method of claim 55 comprising: (a) coating the surface of said substrate with a candidate ligand or target cells expressing a candidate ligand; (b) moving a fluid across the substrate to create shear flow conditions; (c) introducing pathogens or soluble pathogen adhesins into said moving fluid; and (d) observing adhesive interactions between said pathogens and said coated substrate under shear flow conditions to identify pathogen-ligand adhesive interactions" and

changing the bond stress of the isolated adhesion so that the bond stress increases under shear force flow conditions (see claims 55-56 and Table 1, page 5; Example 14, page 17, and table on page 17-18; Example 16; tables on page 20-21, especially the Microbial Pathogen carbohydrate binding protein that bind to carbohydrate ligand.)

Bargatze et al still anticipates the instantly claimed invention as now claimed as the claimed methods steps may be carried out in any order "comprising", as well as carried out in the claimed order, as Bargatze et al evaluate the bond strength under shear flow stress conditions between an adhesion and ligand which are bound to each other.

3. Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594

4. Inherently the reference anticipates the now claimed invention. Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior arts functioning, does not render the old composition patentably new to the discoverer. AThe Court further held that Athis same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art.

3. The rejection of claims 1-2, 4, 6-7 under 35 U.S.C. 102(b) as being anticipated by Brooks et al (1983) is traversed on the grounds that:

c. The reference does not disclose an isolated force activated stress dependent adhesion molecule or a force activated stress dependent binding ligand as required by the claims.

4. It is the position of the examiner that Brooks isolated Aeromonas salmonicida strain 438 which comprises the adhesion, and contacted the isolated adhesion with its ligand attached to a particle, specifically erythrocytes under shear stress.

Applicant's definition of I-FASDAM includes " [0111] In the practice of this invention, a FABSDAM or an isolated FABSDAM (I-FABSDAM) and/or a FASBSDB-L can be attached to a particle, including, but not limited to bacterial pili, naturally occurring isolated molecules, synthetic molecules, proteins, polypeptides, organelles, prokaryotic cells to which said FABSDAM is not native, eukaryotic cells to which said I-FABSDAM is not native, viruses, organisms, nanoparticles, microbeads, and microparticles or to a surface selected from the group consisting of cell membranes, other biological membranes, device surfaces and synthetic substrate surfaces."

Brooks et al still anticipates the instantly claimed invention as now claimed.

Original Prior art rejection: Brooks et al disclose the instantly claimed invention directed to a method comprising the step of increasing the bond strength (see page 320, paragraph 2, last full sentence; page 321, paragraph 1 "This second phase represents a marked strengthening of the aggregation and hence of bacterial adhesion induced by shear in the system") of an isolated adhesion of E.coli pili, wherein the increase in bond strength was induced by shear force (see page 327, Figure 10 and page 328, Figure 11), and wherein the ligand was A+ human erythrocytes that are known to present D-mannose/L-fucose carbohydrate ligand (see figure 2, ledger, line 3 and Figure 2 alphaMM defined at page 321, paragraph 2, line 5). Brooks et al anticipates the instantly claimed invention as now claimed.

Conclusion

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on flextime, but usually M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Vgp
November 19, 2007

MARK NAVARRO
PRIMARY EXAMINER